Individual or Combined Effects of Enalapril and Verapamil on the Chronic Cyclosporine Nephrotoxicity in Rats

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Previous studies have demonstrated that enalapril or verapamil seems to attenuate the cyclosporine nephrotoxicity. However, the effect of individual or combined treatment on the osteopontin, TGF-β, endothelin-1 and procollagen alpha 1(I) gene expressions, which have been implicated in the pathogenesis of cyclosporine nephrotoxicity, has not been known much. Enalapril(50mg/L in drinking water) and verapamil(0.5mg/kg/day), subcutaneously), alone or in combination, were administered to rats with chronic cyclosporine nephrotoxicity(cyclosporine, 25mg/kg/day, subcutaneously)(each n=5). 5 rats treated with olive oil vehicle were served as normal. After 4 weeks, biochemical parameters were measured and renal cortical mRNA levels were evaluated by Northern blot analysis. Cyclosporine reduced the renal creatinine clearance significantly and induced the renal cortical osteopontin, TGF-β, endothelin-1 and procollagen alpha 1(I) gene expressions around 13.5±1.3, 2.4±0.2, 1.5±0.1, 1.9±0.1 folds respectively. Individual treatment with enalapril or verapamil significantly suppressed the cyclosporine-induced osteopontin and TGF-β mRNA expression, but not endothelin-1 and procollagen alpha 1(I). Combined treatment also inhibited the osteopontin and TGF-β mRNA expression but there was no difference between combined treatment and each individual treatment. In conclusion, enalapril or verapamil significantly blunted the cyclosporine-induced osteopontin and TGF-β gene expressions. However, combined treatment did not show any additive effects.